

# Isolated disease of left anterior descending coronary artery

## *Angiocardigraphic and clinical study of 218 patients*

NICHOLAS BROOKS, MARTIN CATTELL, KEVIN JENNINGS,\* RAPHAEL BALCON, MICHAEL HONEY, CLIVE LAYTON

*From Cardiac Department, London Chest Hospital, Bonner Road, London*

**SUMMARY** The angiocardigraphic and clinical findings in 218 patients with significant obstruction confined to the left anterior descending coronary artery were reviewed to study the influence of the site of obstruction and of the collateral circulation on clinical presentation and prognosis. One hundred and fifty-six patients had been managed medically, 51 had had aortocoronary bypass operations, and 11 had had left ventricular aneurysms excised.

The artery was divided into three segments: left anterior descending 1 (LAD1) from its origin to the first septal branch, left anterior descending 2 (LAD2) from the first septal to the first diagonal branch, and left anterior descending 3 (LAD3) the remaining distal vessel.

Cardiogenic shock occurred only in patients with LAD1 lesions, but apart from this the clinical presentation bore no consistent relation to the site of disease. Patients with proximal lesions were more likely to have a "positive" exercise test, had more severely impaired left ventricular function, and had a worse prognosis than those with more distal disease. Non-visualisation of collateral vessels in patients with left anterior descending occlusion was associated with extensive infarction, and patients who presented with infarction had more severely impaired ventricular function than those who presented with angina and subsequently had an infarction. Left ventricular function was poor at the time of angiography in 11 of 12 of those who subsequently died; it is therefore unlikely that the prognosis of patients with isolated left anterior descending obstruction could be improved by expanding the indication for aortocoronary bypass from that of severe angina.

The notion that a proximal obstruction in a coronary artery is more dangerous than an obstruction distal to one or more of its major branches is logical, but difficult to prove because of other factors influencing the outcome in an individual patient. With the exception of left main stem lesions, the emphasis of much diagnostic activity in recent years has been directed to the assessment of patients according to the number of diseased vessels and the severity of obstruction rather than its site. "Significant" obstruction confined to one coronary artery is a common angiographic finding<sup>1-4</sup> which provides an opportunity to study the influence of arteriosclerotic lesions at different levels in the coronary artery tree. Because of their numerical pre-

ponderance<sup>2-4</sup> and a less certain prognosis in comparison with others with "single vessel disease"<sup>3 5 6</sup> we have examined a group of patients with greater than 50% reduction in diameter confined to the left anterior descending artery.

### **Patients and methods**

Since 1971, clinical information and details of coronary arteriograms carried out on patients investigated at the London Chest Hospital have been recorded on mark-sense cards and stored in a computer. From this we have retrieved details of all patients with greater than 50% reduction in diameter of the left anterior descending artery (including those with additional diagonal branch disease), but with the left circumflex and right coronary arteries and their branches, and the left main stem, normal or stenosed by less than

\*Present address: Department of Cardiology, Freeman Hospital, Newcastle-Upon-Tyne, NE7 7DN.

50%. Patients living outside the United Kingdom were excluded. The final study group comprised 218 patients, 180 men and 38 women, aged 27 to 71 (mean 50) years.

Angina was graded on a scale of 1 to 4, grade 1 being angina occurring only with severe exertion, grade 2 during normal activities, grade 3 with minimal exertion, and grade 4 at rest (with or without additional effort angina). The electrocardiogram was regarded as showing evidence of previous infarction if there were pathological Q waves, or a progressive reduction in R wave amplitude in the chest leads ("poor R wave progression"). A history of infarction was accepted even in the absence of these electrocardiographic changes at the time of investigation. For patients not followed up by ourselves information was obtained whenever possible from the family doctor or referring physician. All were "tagged" with the Registrar of Births and Deaths so that follow-up with respect to mortality is complete to January 1980, unless death occurred outside the United Kingdom.

#### ANGIOGRAPHIC ANALYSIS

The left coronary artery injections were made in posteroanterior, right anterior oblique 30°, and left anterior oblique 60° projections, and the right coronary in at least two of these. The anterior descending artery from its origin to the first septal branch was designated LAD1, from the first septal to the first diagonal branch LAD2, and the remainder of the distal vessel LAD3. In six patients the diagonal branch was proximal to the first septal branch and in these LAD1 was taken to the origin of the diagonal, and LAD2 from the diagonal to the first septal. In some patients the left main stem divided into three vessels: the main circumflex, the anterior descending, and a "trifurcation" vessel. In four patients this "trifurcation" branch supplied the anterolateral wall of the left ventricle (that is diagonal territory), and the anterior descending artery was considered to have only two segments, LAD2 and LAD3, whose junction was the first septal branch. Four patients with both LAD3 and diagonal lesions were classified as having LAD2 disease. The extent of reduction of diameter in each segment was measured. In making subsequent comparisons between patients with disease in different sites, those with multiple left anterior descending lesions were classified according to the most proximal obstruction of greater than 50%. The presence or absence of collateral channels, and whether or not the artery distal to an occlusion was seen, were also recorded.

The left ventricle was assessed from the 30° right anterior oblique ventriculogram. Ejection fraction was determined using a planimeter; ectopic and post-ectopic beats were not analysed. The outline of the

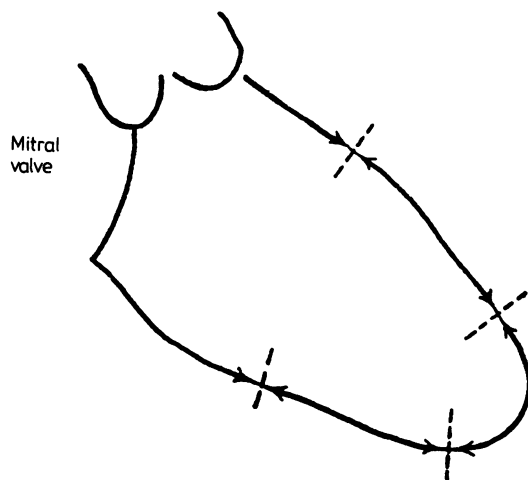


Fig. 1 Diagram of left ventriculogram in 30° right anterior oblique projection showing division of the wall into five segments.

ventricle was divided into the five segments illustrated in Fig. 1<sup>7</sup> and each was designated as showing normal contraction, hypokinesia, akinesia, or dyskinesia in systole.

#### STATISTICAL ANALYSIS

Means and proportions were compared by calculation of the standard error of the difference, and an actual difference of greater than twice the standard error was accepted as significant ( $p < 0.05$ ). The  $\chi^2$  test was used where appropriate.

#### Results

##### ANGIOCARDIOGRAPHIC FINDINGS

The anterior descending artery was occluded in 101 patients (with or without a stenosis proximal to the occlusion), and narrowed by 90% of its diameter in 40, 80% in 24, 70% in 21, 60% in 12, and 50% in 20. The most proximal major lesion (greater than 50%) was in LAD1 in 81 patients, LAD2 in 104, and LAD3 in 33. Additional irregularities or minor stenoses (range 10 to 40%) were present in the right or circumflex arterial systems in 142 patients.

Satisfactory measurements of left ventricular ejection fraction were made for 201 patients. The mean ejection fraction was 59.2% (SD 19.2) in 74 with LAD1 lesions, 61.2% (SD 20.2) in 95 with LAD2 lesions, and 68.4% (SD 12.0) in 32 with LAD3 disease. The difference in mean ejection fraction between those with LAD1 and LAD2 disease is not statistically significant, but those between patients with LAD1 and LAD3 disease, and between those with LAD2 and LAD3 disease are significant

( $p < 0.05$ ). Analysis of segmental wall motion disclosed a similar trend: the average number of abnormally contracting segments was 1.35 in the 81 patients with LAD1 lesions, 1.04 in the 104 with LAD2 lesions, and 0.58 in the 33 with distal (LAD3) disease. This progressive increase in the number of abnormal segments with more proximal obstruction is highly significant ( $p < 0.01$ ).

In patients with previous infarction (based on the history or the electrocardiogram, or both) left ventricular function was more severely impaired, though the variation was wide. For the three groups, LAD1, LAD2, and LAD3 mean ejection fractions were 48.0% (SD 18.3) ( $n=40$ ), 53.7% (SD 19.9) ( $n=44$ ), and 68.2% (SD 15.4) ( $n=13$ ), respectively (LAD1—LAD2 difference not significant, LAD2—LAD3  $p < 0.01$ ). The corresponding mean numbers of abnormally contracting segments were 2.13 ( $n=42$ ), 1.82 ( $n=45$ ), and 1.08 ( $n=13$ ) ( $p < 0.01$ ). Thirty-two patients, all with left anterior descending occlusion, had left ventricular aneurysms; in 11 the obstruction was in LAD1, in 19 it was in LAD2, and in two in LAD3. Left anterior descending occlusion was not invariably associated with clinically recognisable myocardial necrosis: 18 patients with occlusion (eight LAD1, five LAD2, and five LAD3) had no history or electrocardiographic evidence of infarction, and had normal ventriculograms.

#### CLINICAL PRESENTATION

In 73 patients (33%) the first manifestation of heart disease was a myocardial infarction. One hundred (46%) presented with exertional angina pectoris, 35 (16%) with angina at rest, two (1%) with breathlessness, and eight (4%) with "atypical" chest pain. At the time of angiography 164 had angina, 14 complained predominantly of breathlessness, eight had "atypical" pain, and 29 were symptom free. Three of the patients who presented with myocardial infarction were in cardiogenic shock. One hundred patients had at some time had a myocardial infarction.

In patients with angina at the time of coronary angiography there was no discernible relation between its severity and the site of left anterior descending obstruction; rest pain, for example, was present in 21% (12/57) of patients with LAD1, 21% (17/81) with LAD2, and 23% (6/26) with LAD3 lesions. By contrast, and consistent with the angiocardiographic analysis, clinical evidence of left ventricular failure was more common with proximal coronary obstruction: 12% of patients (10/81) with LAD1 disease were in left ventricular failure (three had cardiogenic shock), compared with 7% (seven/104) with LAD2, and 3% (one/33) of the LAD3 patients.

The resting electrocardiogram was normal in 82 patients (38%). In 60 (28%) there were ST segment or

T wave changes, of whom two with T wave inversion in leads V1-V4 had complete right bundle-branch block. Q waves or poor R wave progression were present in 73 cases (33%) and in six this was associated with complete right bundle-branch block. One patient had complete atrioventricular block, and two were in atrial fibrillation. The proportion with electrocardiographic changes of infarction at the time of angiography was related to the site of the most proximal anterior descending lesion: 47% of patients (38/81) with LAD1 disease had these changes compared with 27% (28/104) of those with LAD2, and 21% (seven/33) of those with LAD3 obstruction ( $p < 0.01$ ).

#### EXERCISE TESTING

Symptom limited graded exercise tests were carried out on a bicycle ergometer in 109 patients before cardiac catheterisation. Lead I of the electrocardiogram was monitored continuously and recorded at the end of each stage. The results are given in Table 1. In 25 of 41 patients (61%) with LAD1 lesions exercise was terminated by chest pain, 1 mm or greater ST segment depression 0.08 s after the end of the QRS complex, or by both pain and ST segment change. By contrast, only 21 of 51 patients (41%) with LAD2 lesions, and five of 17 (29%) with LAD3 lesions had these end-points ( $p < 0.05$ ). The mean peak load was not significantly different between the three groups of patients.

#### COLLATERAL CIRCULATION

In seven patients of 101 with left anterior descending occlusion the distal vessel did not opacify during angiography, and no collateral vessels were seen. Left ventricular function was severely impaired in these patients including the three in cardiogenic shock: the mean ejection fraction was 28% (range 10 to 41%), and all had two or more abnormally contracting segments.

In the other 94 patients with occluded arteries the distal vessel was visualised during the left coronary injection. In 77 of these the vessel also opacified by visible collateral channels from the right side (or from the left, when the right coronary artery was non-

Table 1 Exercise testing in 109 patients

	LAD1	LAD2	LAD3
Mean peak load (kpm/min)	582	623	609
End-point			
Chest pain	11(2)	11(4)	3(0)
Dyspnoea	15(5)	22(6)	6(1)
Fatigue	13(7)	16(4)	6(1)
Other	2(2)	2(0)	2(0)
Total	41(16)	51(14)	17(2)

Figures in parentheses are patients with ST segment depression.

dominant). Most commonly these vessels were in the septum arising from the posterior descending artery, but in some cases an enlarged conus artery or a vessel around the cardiac apex in direct continuity from posterior to anterior descending arteries comprised the main collateral communication.

Collateral vessels were never seen in patients with less than 70% stenosis of the left anterior descending artery, even in the presence of clear historical, electrocardiographic, or ventriculographic evidence of previous infarction. Such communications opacified in one of 21 patients with 70% stenosis, in two of 24 with 80% stenosis, in 13 of 40 with 90% stenosis, and in 77 of 101 with occlusion. This tendency for the more frequent demonstration of collateral circulation with increasing arterial obstruction is highly significant ( $p < 0.01$ ).

Left ventricular function in patients having left anterior descending occlusion with opacified collateral channels was compared with that in patients with occlusion and no visible collateral circulation other than "ghosting" of the distal vessel. The mean ejection fraction was 59.2% (SD 17.5) in 73 patients with collaterals, and 44.7% (SD 25.5) in 17 without; the difference is significant ( $p < 0.05$ ). Wall motion analysis disclosed a similar difference: patients with visible collaterals had an average of 1.47 abnormal segments compared with 2.23 in those without ( $p < 0.05$ ).

There was no discernible relation between the demonstration of collateral vessels and the severity of angina. Of the patients with angina and opacified collaterals, 21% (15/71) had pain at rest, compared with a 23% (21/93) incidence of rest pain in those without collaterals on the angiogram. It should, however, be emphasised that eight of the 21 patients with rest pain and no demonstrable collaterals had left anterior descending stenoses of less than 80%.

It is widely believed that collateral vessels can grow in response to chronic ischaemia from slowly progressive arterial obstruction, thereby protecting the myocardium when occlusion finally occurs. An indirect attempt to examine this assumption was made in the patients with infarction and left anterior descending occlusion by comparing left ventricular function between those who presented with their infarction and those whose first clinical event was angina. In 49 patients presenting with infarction the mean ejection fraction was 44.2% (SD 20.6) compared with 56.6% (SD 9.6) in 23 patients in whom angina preceded infarction ( $p < 0.01$ ).

#### FOLLOW UP

Fifty-one patients (19 LAD1, 28 LAD2, and four LAD3) with severe angina (mean grade 2.8, 15 rest pain) had vein grafts to the anterior descending

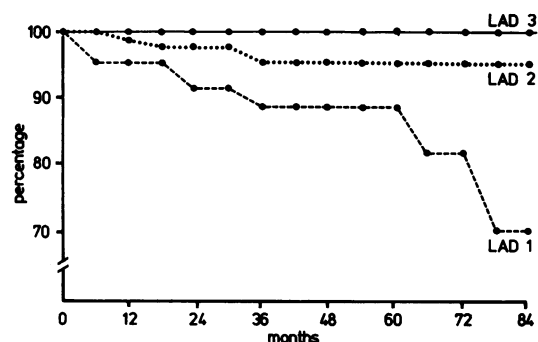


Fig. 2 Survival curves of the patients classified according to the site of the most proximal anterior descending artery obstruction.

artery. There were no perioperative deaths or electrocardiographically recognised myocardial infarctions. One patient had a non-fatal inferior infarct 33 months after operation, one died suddenly after 77 months, and another died from carcinoma of the bronchus. At follow up three to 84 (mean 39) months after angiography, 38 (75%) were symptom free or had improved by at least two grades. Eleven patients (eight LAD1 and three LAD2) had left ventricular aneurysms resected; a patient with cardiogenic shock died 10 days after operation, and another died after 61 months. Six were symptomatically improved at follow-up.

Conservative management was adopted for the other 156 patients. Detailed follow-up information (three to 84, mean 24 months) is available on 99 of those who had angina at the time of angiography; 71% (22/31) of those with LAD1, 52% (24/46) with LAD2, and 82% (18/22) with LAD3 disease were symptom free or improved. Nine medically treated patients died, all from their heart disease. In six the most proximal obstruction was in LAD1, and in three in LAD2 (one LAD2 equivalent); none with disease confined to the distal vessel died. In general the left ventricular function of those who died was poor at the time of cardiac catheterisation: their mean ejection fraction was 38% (range 10 to 83%), and they had an average of 2.64 abnormally contracting segments. Four, including two with cardiogenic shock, had severe left ventricular failure.

Details of patients who died (excluding the non-cardiac death) are given in Table 2, and the combined medical and surgical survival curves are plotted in Fig. 2. Overall, nine out of 81 patients (11%) with LAD1 disease died compared with three out of 104 (3%) with LAD2 disease, and none of the 33 with distal lesions. Despite the small number of deaths, the difference in mortality between LAD1 and LAD2

Table 2 Mortality: clinical and angiographic details

LAD lesion	LV function		Presentation	Electrocardiogram	Survival (mth)	Collaterals	Comments
	Ejection fraction (%)	No. of abnormal segments					
1	1 occlusion	50	3	AP 3	Poor R	33	Present
2	1 occlusion	29	3	MI, CS	Q	0	Absent
3	2 occlusion	10	3	MI	Poor R	35	Present
4	2 80%	47	3	MI	T inversion	10	Absent
5	1 occlusion	52	2	AP 3	Q	20	Present
6	1 occlusion	10	3	MI, CS	Q	0	Absent
7	* 3 occlusion diag. 70%	83	0	AP 3	T inversion	14	Present
8	1 70% 2 occlusion	52	2	AP 2	CHB	0	Present Paced
9	1 occlusion	27	3	MI	Poor R	23	Present
10	1 occlusion	21	3	MI, CS	Q	0	Absent
11	1 occlusion	38	4	MI	Q	61	Present
12	1 occlusion	34	3	MI	Q	77	Present

\*LAD 2 equivalent; diag., diagonal branch; AP, angina pectoris; MI, myocardial infarction; CS, cardiogenic shock; Q, anterior Q waves; CHB, complete heart block.

patients, and between both LAD1 and LAD2, and LAD3 is statistically significant ( $p < 0.05$ ).

## Discussion

In this study of patients with clinically manifest coronary disease confined to the anterior descending artery, those with proximal lesions had on average greater impairment of left ventricular function than those with more distal obstruction. These observations confirm those of two recently reported studies of patients with anterior myocardial infarction from which it was concluded that the site of left anterior descending obstruction was a primary determinant of the size of the infarction.<sup>8,9</sup> We have shown in addition that the prognosis of our patients was related to the site of the obstruction, but because some had surgical treatment which might itself have influenced the outcome, we cannot be certain that this represents the untreated natural history. To alter this relation, however, surgery would have had to prevent death in patients with distal lesions, and this seems unlikely. The worse prognosis of left anterior descending obstruction proximal to the first septal branch in comparison to that of more distal lesions is well recognised,<sup>10,11</sup> but has not previously been shown to hold for patients with disease confined to the left anterior descending artery.

Despite overall differences in left ventricular function (and indirectly in prognosis) between patients with obstruction in different parts of the left anterior descending artery, a number with proximal occlusion had little or no ventricular damage while others with distal disease had had extensive infarctions. Two questions remain unanswered: what factors other than the site of obstruction determine the potential area of

infarction, and is it logical to expect that by expanding the indications for aortocoronary bypass surgery the prognosis could be improved?

One possible explanation for the great variability in extent of myocardial necrosis which accompanies left anterior descending occlusion is that the functional capacity of the collateral circulation might vary from one person to another, and indeed from one moment to another in the same patient. Though there were patients with "good" collaterals and extensive infarction we observed an overall association between the failure of their angiographic opacification and severe left ventricular damage. Similar observations have been made by other authors,<sup>12-14</sup> but we believe that their assumption of a cause and effect relation between angiographically assessed "inadequate collateral vessels" (sic)<sup>12</sup> and extensive infarction may be an oversimplification. Widespread necrosis might result in destruction of collateral vessels or of the capillary bed they perfuse, or in their functional closure because of the lower metabolic demand of fibrous tissue compared with that of contracting myocardium. Furthermore, collateral filling might not occur because the perfusion pressure (the difference between proximal and distal coronary pressure) at the time of angiography was not sufficiently high—this could arise from a low arterial pressure, from a high left ventricular diastolic pressure (present in the patients with "inadequate collateral vessels" described by Williams *et al.*<sup>14</sup>), or from a combination of the two. In support of this theory is our observation that collateral vessels were never seen when the left anterior descending stenosis was less than 70% (distal coronary pressure too high). Furthermore, when coronary stenoses are treated by angioplasty collateral vessels immediately "disappear" with relief of

the obstruction and they may "appear" promptly with the development of occlusive coronary artery spasm. These considerations together with our inability to discern a relation between the severity of angina and demonstrable collateral filling suggest that angiographic visualisation of the collateral circulation discloses limited information concerning its functional potential.

On the other hand, the observation that left ventricular function was more severely impaired in patients with left anterior descending occlusion who presented with infarction than in those who presented with angina and subsequently had an infarction supports the belief, based on post-mortem studies,<sup>15 16</sup> that collateral vessels can increase in size in response to slowly developing ischaemia, and that they confer a protective effect. Finally, it is possible that the occurrence and extent of necrosis caused by closure of a coronary artery is dependent also on the autonomic and consequent haemodynamic disturbances accompanying the event, which influence not only collateral flow, but also the myocardial oxygen consumption.

Because this is a retrospective study and 30% of the patients had operations, we are not in a position to draw more than the most tentative conclusions about the role of surgery. There is, however, nothing to support the view that aortocoronary bypass would improve the prognosis of those with proximal lesions who are symptom free or who have only mild angina. Mortality is related to left ventricular function and 11 of the 12 patients who died had angiographic evidence of extensive infarction (two or more abnormally contracting segments) at the time of presentation and investigation. Only one patient with a normal left ventricular angiogram died. It is possible that the prognosis of the 51 patients with severe angina who had vein grafts has been improved by the operation. In view of the undoubted benefit of surgical treatment in terms of pain relief, however, it is doubtful whether such a proposition can ever be put to the test of a formal trial.

The short-term prognosis for most patients with isolated disease of the anterior descending artery is, therefore, good, a conclusion that confirms earlier reports. The outcome is influenced by the site of obstruction, and may be ameliorated by growth of the collateral circulation stimulated by recurrent ischaemia. Severity of angina at presentation is not a good indication of the site of left anterior descending disease, though exercise testing may give useful information. While our findings support the view that management of patients with coronary disease should be governed by the amount of myocardium at risk, a factor determined only in part by the number of vessels involved, there is no evidence to support the contention that isolated proximal anterior descending

artery obstructions should be bypassed unless this is required for relief of limiting angina.

## References

- 1 Bruschke AVG, Proudfit WL, Sones FM Jr. Progress study of 590 consecutive non-surgical cases of coronary disease followed 5-9 years. I. Arteriographic correlations. *Circulation* 1973; 47: 1147-53.
- 2 Moraski RE, Russell RO Jr, Smith M, Rackley CE. Left ventricular function in patients with and without myocardial infarction and one, two or three vessel coronary artery disease. *Am J Cardiol* 1975; 35: 1-10.
- 3 Burggraf GW, Parker JO. Prognosis in coronary artery disease. Angiographic, hemodynamic, and clinical factors. *Circulation* 1974; 51: 146-56.
- 4 Vieweg WVR, Warren SE, Alpert JS, Hagan AD. The distribution and severity of coronary artery disease and left ventricular dysfunction among patients with single coronary artery disease and angina pectoris. *Clin Cardiol* 1980; 3(4): 241-5.
- 5 Proudfit WL, Bruschke AVG, Sones FM Jr. Natural history of obstructive coronary artery disease: ten-year study of 601 nonsurgical cases. *Prog Cardiovasc Dis* 1978; 21: 53-78.
- 6 Webster JS, Moberg C, Rincon G. Natural history of severe proximal coronary artery disease as documented by coronary cineangiography. *Am J Cardiol* 1974; 33: 195-200.
- 7 A.H.A. Grading Committee Report. A reporting system on patients evaluated for coronary artery disease. *Circulation* 1975; 51: 6-40.
- 8 Kumpuris AG, Quinones MA, Kanon D, Miller RR. Isolated stenosis of left anterior descending or right coronary artery: relation between site of stenosis and ventricular dysfunction and therapeutic implications. *Am J Cardiol* 1980; 46: 13-20.
- 9 Hori M, Inoue M, Ohgita N, *et al.* Site and severity of coronary narrowing and infarct size in man. *Br Heart J* 1980; 44: 271-9.
- 10 Griffith LSC, Platia EV, Angell CS, Grunwald L. Coronary arteriographic and electrocardiographic correlates of sudden cardiac death. *Acta Med Scand* 1977; suppl 615: 43-9.
- 11 Taylor GJ, Humphries JO, Mellits ED, *et al.* Predictors of clinical course, coronary anatomy and left ventricular function after recovery from acute myocardial infarction. *Circulation* 1980; 62: 960-70.
- 12 Levin DC. Pathways and functional significance of the coronary collateral circulation. *Circulation* 1974; 50: 831-7.
- 13 Berndt T, Shettigar UR, Lipton MJ, Hultgren HN. Left anterior descending coronary artery obstruction. Clinical, electrocardiographic, and angiographic correlates. *Br Heart J* 1976; 38: 633-40.
- 14 Williams DO, Amsterdam EA, Miller RR, Mason DT. Functional significance of coronary collateral vessels in patients with acute myocardial infarction: relation to pump performance, cardiogenic shock and survival. *Am J Cardiol* 1976; 37: 345-51.

- 15 Fulton WFM. Arterial anastomoses in the coronary circulation. II. Distribution, enumeration and measurement of coronary artery anastomoses in health and disease. *Scott Med J* 1963; 8: 466-74.
- 16 Fulton WFM. Anastomotic enlargement and ischaemic

myocardial damage. *Br Heart J* 1964; 26: 1-15.

Requests for reprints to Dr N Brooks, The London Chest Hospital, Bonner Road, London E2 9JX.